PERKIN 1

Radical-chain addition of aldehydes to alkenes catalysed by thiols

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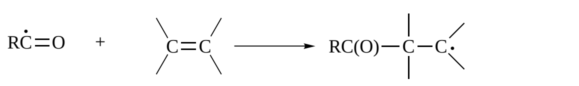
Thiols catalyse the radical-chain addition of primary aliphatic aldehydes R^1CH_2CHO to terminal alkenes $H_2C{=}CR^2R^3$ to give ketonic adducts $R^1CH_2C(O)CH_2C(H)R^2R^3$ in moderate to good yields. The reaction takes place under mild conditions (dioxane solvent, 60 °C) and is initiated by di-*tert*-butyl hyponitrite (TBHN). Thiol catalysis is effective for hydroacylation of electron-rich, -neutral and -deficient alkenes, but is most efficient for addition to electron-rich double bonds. For example, the addition of butanal (2 equiv.) to isopropenyl acetate [$H_2C{=}C(Me)OAc$] in the presence of TBHN (2 × 2.5 mol%) and methyl thioglycolate (MeO_2CCH_2SH; 2 × 5 mol%) gives the adduct in 80% yield, whilst a similar reaction in the absence of thiol catalyst affords only an 8% yield. Other enol acetates, silyl enol ethers, an enol phosphate and butyl vinyl ether react similarly. For comparison, the reaction of butanoyl phenyl selenide with isopropenyl acetate, in the presence of tributyltin hydride and azoisobutyronitrile initiator in benzene at 80 °C, gives the adduct in only 7% yield. Methyl thioglycolate is generally the most efficient catalyst for hydroacylation of electron-rich alkenes, whilst *tert*-dodecanethiol is more effective for addition of aldehydes to electron-deficient alkenes. Triorganosilanethiols also function as catalysts, as does the arenethiol 2,4,6-tris(trifluoromethyl)thiophenol. The role of the thiol is to act as a polarity-reversal catalyst that promotes the overall hydrogen-atom transfer from the aldehyde to the carbon-centred radical produced by addition of the acyl radical to the alkene. Intramolecular hydroacylation is also subject to thiol catalysis and the radical-chain cyclisation of citronellal to a mixture of menthone and isomenthone is effectively promoted in the presence of triphenylsilanethiol.

Inter- and intra-molecular addition of acyl radicals to carbon–carbon multiple bonds has become an established method for C–C bond formation.[1] The intramolecular addition has been elegantly exploited in recent years as a key ring-forming process in organic synthesis, particularly in the hands of Boger,[2] Crich,[3] Curran[4] and Pattenden.[5] Several types of compound have been used successfully as acyl radical precursors, including acyl halides,[2d,6] acylcobalt(III) derivatives,[7] acyl aryl selenides[8] and acyl aryl tellurides.[3a,9]

Inter- and intra-molecular radical-chain hydroacylation of alkene functions is commonly accomplished using acyl aryl selenides in the presence of tin hydrides, usually tributylstannane; the propagation sequence involved is shown in eqns. (1)–(3).

$$Bu_3Sn^{\bullet} + RC(O)SePh \longrightarrow Bu_3SnSePh + R\dot{C}{=}O \quad (1)$$



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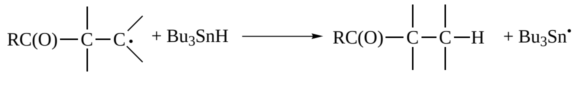

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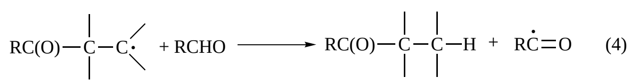
Acyl radicals are nucleophilic species[1,2,10] and, as was emphasised long ago by Walling in his seminal monograph,[11] polar effects are very important in the addition of acyl radicals to C=C bonds. For example, while the $RC(O)SeAr–Bu_3SnH$ couple gives good yields of hydroacylation products with electron-deficient alkenes,† yields from electron-rich or unactivated alkenes are usually poor,[2d] probably because of slow acyl-radical addition to the C=C bond [eqn. (2)]. Competitive trapping of the acyl radical by the tin hydride occurs to give the aldehyde as a major by-product, even when steps are taken to keep the [alkene] : [Bu_3SnH] ratio high by using excess alkene and adding the tin hydride slowly using a syringe pump.

The hydroacylation of an alkene by the direct radical-chain addition of an aldehyde across the C=C bond, *via* the propagation cycle of reactions (2) and (4), was first reported by



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Kharasch *et al.* nearly 50 years ago.[13] Subsequently, this method of hydroacylation has been used quite widely for intermolecular[14,15] and intramolecular[16,17] formation of carbon–carbon bonds and the reaction has been reviewed on a number of occasions.[1,11,18] Provided that the adduct radical **1** is not strongly stabilised (which could render hydrogen-atom abstraction from the aldehyde appreciably endothermic and thus prohibitively slow), hydroacylation is most successful for addition to electron-deficient double bonds, on account of favourable polar effects on both of the elementary steps (2) and (4); homolytic addition to an electron-deficient alkene necessarily affords a relatively electrophilic radical **1** and thereby favours abstraction of hydrogen from the aldehyde [eqn. (4)].[11,14g,19] In general, hydroacylation by this method is applicable only for the addition of primary aldehydes (RCH_2CHO); with secondary, or especially tertiary, aldehydes the reaction is complicated by decarbonylation of the acyl radical which competes with its addition to the C=C bond.

Waters and his co-workers[20] showed many years ago that the radical-chain decarbonylation of aldehydes to give alkanes is catalysed by thiols.[21] The uncatalysed reaction is sluggish because the second step of the propagation cycle [eqns. (5) and (6)] involves abstraction of hydrogen from the aldehyde by a

$$R\dot{C}{=}O \longrightarrow R^{\bullet} + CO \quad (5)$$

$$R^{\bullet} + RCHO \longrightarrow RH + R\dot{C}{=}O \quad (6)$$

† The rate constant for addition of the pivaloyl radical $Bu^t\dot{C}{=}O$ to the electron-deficient alkene acrylonitrile ($H_2C{=}CHCN$) is 5×10^5 dm^3 mol^{-1} s^{-1} at 27 °C.[12]

relatively nucleophilic alkyl radical, a reaction which is not promoted by polar effects.[19] In the presence of a thiol, this step is replaced by the catalytic cycle of reactions (7) and (8), both of which benefit from favourable polar effects because the thiyl radical $XS^{\bullet}$ is electrophilic.[19] We have referred to the general principle embodied in this process as *polarity-reversal catalysis*[22] and we have demonstrated that thiols also catalyse the abstraction of hydrogen from the Si–H group of a trialkylsilane by an alkyl radical, through a cycle of reactions analogous to (7) and (8) in which the aldehyde is replaced by a silane.[23]

$$R^{\bullet} + XSH \longrightarrow RH + XS^{\bullet} \qquad (7)$$

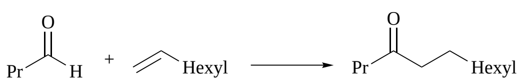
$$XS^{\bullet} + RCHO \longrightarrow XSH + R\dot{C}{=}O \qquad (8)$$

We reasoned that thiols should also catalyse the radical-chain addition of aldehydes to alkenes, in particular to electron-rich and electrically-neutral alkenes, reactions which generally fail because of adverse polar effects on the abstraction of hydrogen from the aldehyde by the now *nucleophilic* adduct radical **1**. In a preliminary communication[24] we reported that thiols do indeed catalyse the hydroacylation of electron-rich alkenes and, in the present paper, we examine the scope of this reaction and present a full account of the earlier work.

Results and discussion

A solution in dry dioxane containing freshly-distilled butanal (5.0 mmol), oct-1-ene (2.5 mmol) and di-*tert*-butyl hyponitrite[25] (TBHN; 0.063 mmol, 2.5 mol% based on alkene) was heated at 60 °C and stirred under argon for a total of 3 h, with a further addition of TBHN (2.5 mol%) after the first hour. The TBHN serves as a thermal source of *tert*-butoxyl radicals at moderate temperatures ($t_{\frac{1}{2}}$ = 55 min at 60 °C), as shown in eqn. (9). Under these conditions, ^{1}H NMR spectroscopic analysis showed that dodecan-4-one had been formed in 24% yield [eqn. (10)]. However, when the experiment was repeated under the same conditions except that methyl thioglycolate (MeO_2CCH_2SH, MTG, 5 mol% based on alkene) was added at the start of the reaction and again at the same time as the second portion of TBHN, the yield of dodecan-4-one more than doubled to 67%. The thiol-catalysed hydroacylation evidently proceeds by the radical-chain mechanism shown in Scheme 1.

$$Bu^tON{=}NOBu^t \longrightarrow 2Bu^tO^{\bullet} + N_2 \qquad (9)$$



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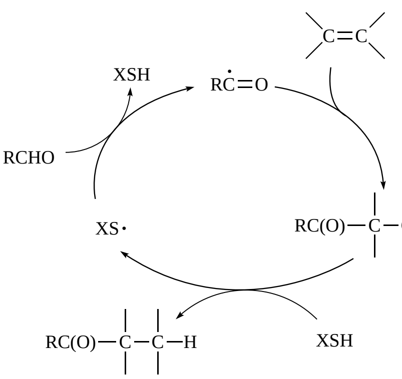
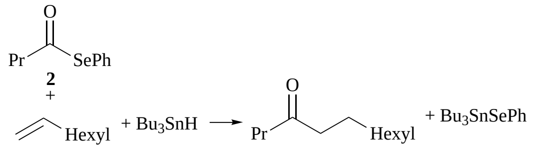


Scheme 1

For comparison, the hydroacylation of oct-1-ene (5.0 mmol) was carried out using butanoyl phenyl selenide **2** (2.5 mmol) in conjunction with tributylstannane (3.7 mmol) at 80 °C in benzene solution, using azoisobutyronitrile (AIBN) as initiator, following the procedure described by Boger [eqn. (11)].[2a,d] The tin



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hydride was added slowly to the reaction mixture using a motor-driven syringe pump, in order to keep the value of [oct-1-ene]/[Bu_3SnH] high throughout. Under these conditions, after all the acyl selenide had been consumed, the yield of dodecan-4-one was 18% and this low value is presumably a reflection of the slow addition of the butanoyl radical to the alkene, coupled with its competitive trapping by the tin hydride to give butanal.

Acyl radicals are strongly nucleophilic[10] and thus the transition state for their addition to a terminal alkene can be described as a hybrid of the canonical structures **3a**–**c**.

$$\left[R\dot{C}(O)\ \ H_2C{=}CHX\right] \longleftrightarrow \left[RC(O){-}CH_2{-}\dot{C}HX\right] \longleftrightarrow \left[R\overset{+}{\dot{C}}(O)\ \ H_2\dot{C}{-}\overset{-}{C}HX\right]$$

3a **3b** **3c**

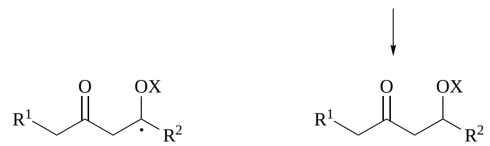
Although general quantitative correlations of the rates of radical addition to alkenes with ground-state properties of the reactants have so far proved rather illusive,[26] the rate of acyl radical addition would be expected to increase with the exothermicity of the reaction (as the radical-stabilising ability of the substituent X increases) and with the contribution from **3c** (as the electron-withdrawing effect of X increases). Kinetic studies of substituent effects on acyl radical addition to alkenes have not been reported,[12] but Fischer and co-workers[26] have carried out extensive quantitative studies of the addition of the nucleophilic radicals $Me^{\bullet}$, $Bu^{t\bullet}$, $HO\dot{C}H_2$ and $Me_2\dot{C}OH$ to a wide range of alkenes and this important work gives support to the qualitative conclusions derived from consideration of the transition state **3**.

Hydroacylation of electron-rich alkenes

The rates of addition of acyl radicals to electron-rich alkenes of the type **5** would not be expected to differ very greatly from the corresponding rates of addition to oct-1-ene.‡ However, the uncatalysed radical-chain addition of an aldehyde **4** across the double bond in **5** would be anticipated to be relatively sluggish, because the *nucleophilic* intermediate adduct radical **7** would be expected to abstract hydrogen from the aldehyde more slowly than does the adduct radical derived from a simple alkene, such as oct-1-ene, and this is already a slow reaction.

4a R^1 = Et
4b R^1 = Hexyl
4c R^1 = Pr^i
4d R^1 = $Bu^tCH_2C(H)Me$
4e R^1 = $MeOCMe_2(CH_2)_4C(H)Me$

5a R^2 = Me, X = Ac
5b R^2 = H, X = Ac
5c R^2 = Bu^t, X = Ac
5d R^2 = H, X = Bu^tMe_2Si
5e R^2 = Bu^t, X = Me_3Si
5f R^2 = Me, X = $(EtO)_2P(O)$
5g R^2 = H, X = Bu



7 **6**

(12)

‡ At 23 °C the relative rates of addition of the highly-nucleophilic $Me_2\dot{C}OH$ to alkenes are $H_2C{=}CHBu^t$ (1), $H_2C{=}CHOEt$ (0.3) and $H_2C{=}CHOAc$ (7.0) [compare the electron-deficient alkene $H_2C{=}CHCO_2Me$ ($> 9.3 \times 10^3$)].[26d]

Table 1 Addition of aldehydes to electron-rich alkenes catalysed by MTG[a] in dioxane at 60 °C in the presence of TBHN[b] (5 mol%)

Entry	Aldehyde	Alkene	Product	Yield (%) by NMR (isolated)
1	**4a**	**5a**	**6aa**	80 (67)
2[c]	**4a**	**5b**	**6ab**	81 (74)
3	**4b**	**5a**	**6ba**	79 (63)
4	**4c**	**5a**	**6ca**	68 (59)
5	**4a**	**5c**	**6ac**	90 (83)
6	**4a**	**5d**[d]	**6ad**	65 (52)
7	**4a**	**5e**	**6ae**	35 (29)
8	**4a**	**5f**	**6af**	36 (29)
9	**4a**	**5g**	**6ag**	66 (58)
10	**4d**	**5a**	**6da**	48 (42)
11	**4e**	**5a**	**6ea**	45 (40)
12[e]	**4a**	*N*-vinylpyrrolidin-2-one	**9**	73 (62)
13[e]	**4a**	*N*-vinylphthalimide	**10**	60 (50)

[a] Methyl thioglycolate (2 × 5 mol%) based on alkene. [b] The TBHN was added in two portions of 2.5 mol% based on alkene. [c] The catalyst was TDT (5 mol% present at the start of the reaction) and the alkene was added slowly using a syringe pump (see text). [d] Described in error as **5** ($R^2 = Bu^t$, $X = Bu^tMe_2Si$) in the Table in ref. 24. [e] TBHN (10 mol% based on alkene) was added in four equal portions of 2.5 mol%.

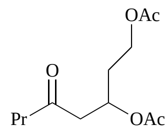
In accord with this analysis, the reaction of butanal **4a** (2 molar equivalents) with isopropenyl acetate **5a** in the absence of thiol, under the conditions described for the hydroacylation of octene (TBHN, 2 × 2.5 mol%) gave the aldol-type produce **6aa**§ in a yield of only 8%. However, in the presence of MTG (2 × 5 mol%) this was raised to 80%. Among other thiols investigated as catalysts for the addition of butanal to isopropenyl acetate under similar conditions were *tert*-dodecanethiol (TDT),¶ triisopropylsilanethiol[27] and triphenylsilanethiol. Of these thiols, MTG was somewhat more effective than the silanethiols (*ca.* 75% yield) and TDT was the least efficient (*ca.* 60% yield). We ascribe the effectiveness of MTG to the presence of the electron-withdrawing methoxycarbonyl group which should favour abstraction of hydrogen from the SH group by the relatively nucleophilic adduct radical **7**. Yields were only slightly improved when 10 mol% TBHN was used as initiator, added in four equal portions, at the start of the reaction and again after 30 min, 1 h and 1.5 h; here the total reaction time was 3.5 h.

The thiol-catalysed hydroacylation of a number of other enol derivatives **5** with the primary aldehydes **4** (2 mol equiv.) was carried out under similar conditions and the results are collected in Table 1. The yields obtained with the straight-chain aldehydes **4a** and **4b** were greater than those from the β-branched aldehydes **4c**–**e**, probably as a result of steric retardation of acyl-radical addition to the alkene. These results highlight how critically dependent is the success of the hydroacylation on the rate of the relatively-slow addition of the acyl radical to the double bond.|| Hydroacylation of enol derivatives using the α-branched aldehyde 2-methylpentanal was unsuccessful, presumably because of ready decarbonylation of the acyl radical coupled with its relatively slow addition to the alkene. Polar solvents are known to retard the decarbonylation of acyl radicals,[28] but still no addition product was formed when the reaction was repeated in acetonitrile solvent.

For comparison, the hydroacylation of **5a** using butanoyl phenyl selenide in the presence of Bu_3SnH was carried out using Boger's procedure, with slow addition of the tin hydride.[2] Only a small amount (7%) of the product **6aa** was obtained and most of the selenide was reduced to butanal. When the experiment was repeated with the more hindered alkene **5c** none of the addition product **6ac** was obtained. The thiol-catalysed addition of aldehydes thus appears to possess significant advantages over the acyl selenide–tin hydride couple for the hydroacylation of electron-rich alkenes.

The TDT-catalysed addition of butanal to vinyl acetate **5b** gave an 8 : 1 mixture of **6ab** together with the 'dimeric' product **8** formed by addition of **7** to a second molecule of alkene, prior to H-atom transfer from the thiol. However, when the alkene was added slowly to the reaction mixture using a syringe pump, the ratio **6ab** : **8** increased to 12 : 1 and the yield of **6ab** was 81% (Table 1, entry 2).

Thiol-catalysed hydroacylation was also effective for enamides, as judged by the ready addition of butanal to *N*-vinylpyrrolidin-2-one and to *N*-vinylphthalimide to give the adducts **9** and **10**, respectively (Table 1, entries 12 and 13). In



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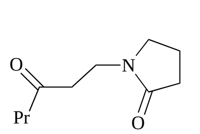

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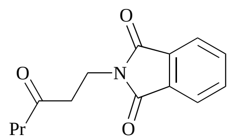

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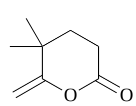
the absence of thiol catalyst, but under otherwise identical conditions, mainly polymeric material and only a trace of **9** were obtained from the reaction of *N*-vinylpyrrolidinone with butanal.

Thiol-catalysed addition of butanal to the cyclic enol esters **11**–**13** was less successful. The methylene lactone **11** afforded very little (*ca.* 5%) of adduct, although hydroacylation with PrC(O)SePh–Bu_3SnH following Boger's procedure gave even less product. The inductive effect of the extra oxygen atom in **12** appears to facilitate the addition and the adduct **14** was



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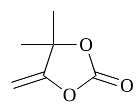

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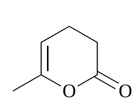

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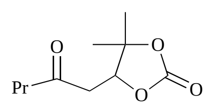

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obtained in 55% yield using Pr^i_3SiSH (2 × 5 mol%) as catalyst; without thiol the yield was 20%. Using Boger's method the yield of **14**, which decomposed on attempted isolation by chromatography over silica gel, was only 8%. Thiol-catalysed addition to **13** failed.

It is noteworthy that thiol-catalysed hydrosilylation[23d] of **11** and **12** gives good yields of addition products.[23e,29] Not only is addition of silyl radicals to alkenes faster than the addition of acyl radicals, but also the β-silyl radical adduct involved should be more nucleophilic than the acyl adduct and probably abstracts hydrogen more rapidly from thiols.

Hydroacylation of electron-deficient alkenes

Other factors being comparable, nucleophilic acyl radicals would be expected to add more rapidly to terminal alkenes that carry electron-withdrawing groups at the allylic position than to oct-1-ene. However, the presence of such groups at the β-position in the resulting radical should not have a large effect on the rate at which this abstracts hydrogen from a thiol or from the parent aldehyde. Hence, such alkenes might be expected to be particularly suitable substrates for thiol-catalysed hydroacylation. Addition of butanal to diethyl allylmalonate **15** was carried out in dioxane at 60 °C (TBHN, 4 × 2.5 mol%; TDT, 2 × 2.5 mol%) and the product **21** was isolated in 65% yield.** In

§ The compound **6aa** is the product of addition of **4a** to **5a** *etc.*

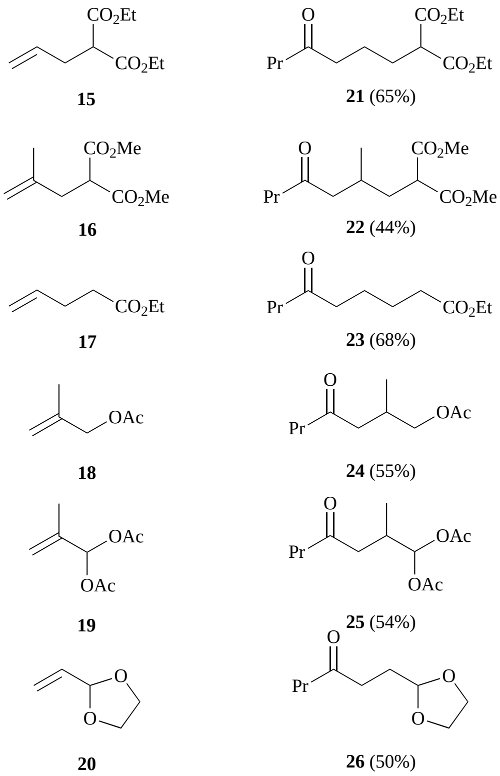
¶ This is the mixture of isomers *tert*-$C_{12}H_{25}SH$ as obtained from the Aldrich Chemical Co.

|| The same problem applies, of course, to hydroacylation using the acyl selenide–tin hydride couple and here the situation is worse because of competitive quenching of the acyl radical by the tin hydride to give aldehyde, which is unreactive in this system.

** In contrast to the hydroacylation of electron-rich alkenes, significantly higher yields of adducts were obtained with 10 mol% TBHN (four additions of 2.5 mol%) than with 5 mol% TBHN (two additions of 2.5 mol%).

the absence of thiol, under otherwise identical conditions, the yield of **21**, determined by ^{1}H NMR spectroscopy, was only 6%. Thus, the thiol catalysis is indeed very efficient.

Additions of butanal to the similarly-substituted alkenes **16**–**20** were carried out using the same procedure with TDT as catalyst and the isolated yields of hydroacylation products are given alongside the formulae in Scheme 2.



Scheme 2 *Reagents and conditions:* TBHN initiator (4 × 2.5 mol%), TDT catalyst (2 × 5 mol%), dioxane solvent, 60 °C, 3.5 h. Isolated yields are shown in parentheses.

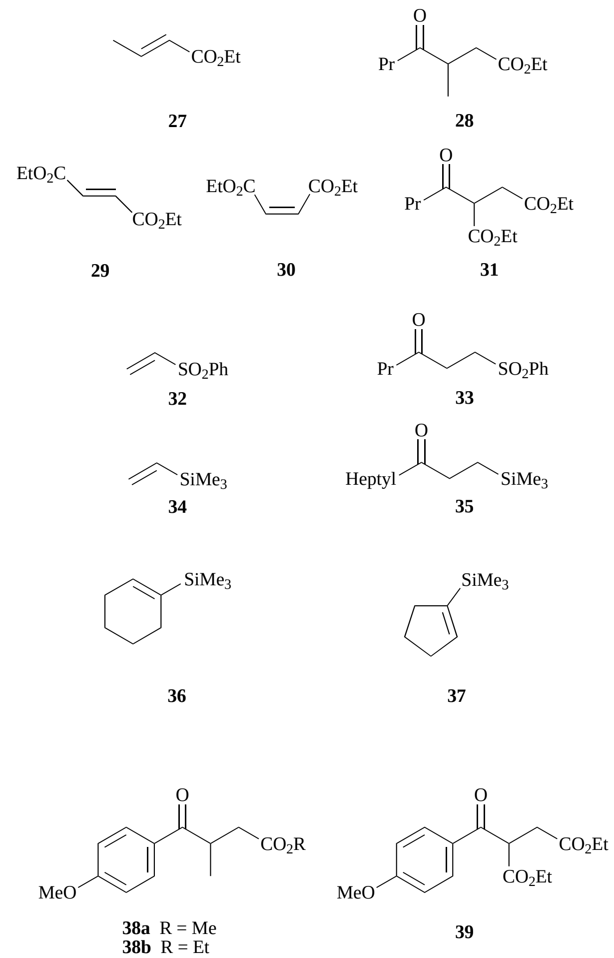
When the electron-withdrawing group is attached directly to the double bond the rate of acyl radical addition should be considerably increased. However, the resulting adduct radical is now relatively electrophilic and will abstract hydrogen relatively rapidly from the parent aldehyde, accounting for the early success of the uncatalysed radical-chain addition of aldehydes to electron-deficient alkenes.[14a,b] An electrophilic adduct radical would be expected to abstract hydrogen less readily from a thiol than does a nucleophilic one, but nevertheless thiol catalysis is still successful in increasing the yield from this type of hydroacylation. Thus, although the reaction of butanal with ethyl crotonate **27** gave the adduct **28** in 42% yield, when TDT (2 × 5 mol%) was used as catalyst this was raised to 95%. Other thiols were investigated as catalysts and the results are summarised in Table 2. As can be seen, MTG was the least effective of thiols examined, in contrast with the results obtained for hydroacylation of the electron-rich alkene **5a**, and this can be attributed to the electrophilicity of the intermediate adduct radical derived from the crotonate. Additions of butanal to diethyl fumarate **29** and to diethyl maleate **30**, in the presence of TDT, gave the adduct **31** in yields of 96 and 93%, respectively. Thiol-catalysed hydroacylation of phenyl vinyl sulfone **32** gave **33** in 56% yield, but while trimethylvinylsilane **34** gave the adduct **35** in 85% yield, the vinylsilanes **36** and **37** afforded only traces of addition products.

Boger has successfully carried out the hydroacylation of electron-deficient alkenes using aroyl aryl selenides in conjunction with tributylstannane.[2] For example, the adduct **38a** was obtained in 76% yield from *p*-methoxybenzoyl phenyl selenide and methyl crotonate.[2d] Addition of *p*-methoxybenzaldehyde

Table 2 Addition of butanal to isopropenyl acetate **5a** and to ethyl crotonate **27** in the presence of different thiols in dioxane at 60 °C

	Adduct yield (%)[b]	
Thiol catalyst[a]	**6aa**[c]	**28**[d]
None	8	42
TDT	62	95
Pr^i_3SiSH	76	98
Ph_3SiSH	70	97
MTG	80	82

[a] Thiol added in two portions of 5 mol% (see text). [b] Yields determined by ^{1}H NMR spectroscopy. [c] The TBHN (5 mol%) was added in two equal portions. [d] The TBHN (10 mol%) was added in four equal portions.



to ethyl crotonate under our conditions (dioxane solvent at 60 °C) gave the corresponding adduct **38b** in 32% yield in the absence of thiol and in 35% yield when TDT (2 × 5 mol%) was present as catalyst. Similarly, addition of this aldehyde to diethyl maleate gave the adduct **39** in 45–50% yield with or without TDT. Catalytic amounts of thiol thus have almost no effect on the yields of these addition reactions. The electrophilic adduct radicals evidently abstract hydrogen at comparable rates from the thiol and from the aromatic aldehyde. In contrast, the adduct radical would be expected to abstract hydrogen very rapidly from a tin hydride, because polar effects are favourable, and it appears that Boger's aroyl aryl selenide–tin hydride couple has a distinct advantage for the overall hydroacylation of electron-deficient alkenes with aromatic aldehydes.

Arenethiols as polarity-reversal catalysts

The strength of the S–H bond in thiophenol (349 kJ mol^{-1}) is significantly less than that in an alkanethiol (366 kJ mol^{-1} in

Table 3 Effectiveness of different thiol catalysts for hydroacylation and hydrosilylation of isopropenyl acetate **5a** in dioxane at 60 °C[a]

Thiol[b]	Aldehyde or silane[c]	Yield of adduct (%)[d]
TDT	PrCHO **4a**	70
TDT	$PhMe_2SiH$	94
PhSH	PrCHO **4a**	<1
PhSH	$PhMe_2SiH$	<1
TFTP	PrCHO **4a**	60
TFTP	$PhMe_2SiH$	92

[a] Reactions were initiated with TBHN (4 × 2.5 mol%). [b] Added in two portions (2 × 5 mol%). [c] Two molar equivalents based on alkene. [d] Yields determined by ^1H NMR spectroscopy.

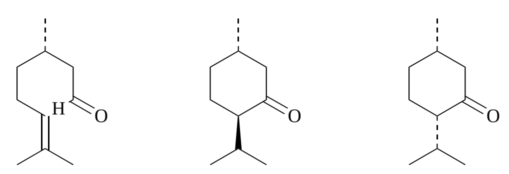
MeSH).[30,31] Consequently whilst thiophenol is an extremely good hydrogen-atom donor towards carbon-centred radicals, the phenylthiyl radical is a poor abstractor of hydrogen from an aldehyde (the dissociation enthalpy[30] of the aldehydic C–H bond in MeCHO is 374 kJ mol^{-1}). Therefore, it would be anticipated that thiophenol would not act as a catalyst for the hydroacylation of alkenes and this was confirmed for the addition of butanal to isopropenyl acetate **5a** (see Table 3): in fact, thiophenol inhibits the reaction. Electron withdrawing groups at *ortho* and *para* positions would be expected to increase the strength of the S–H bond in a substituted thiophenol, as they do for the analogous phenols.[32] Trifluoromethyl groups are strongly electron withdrawing, and have low reactivity in radical reactions, and thus the readily-prepared 2,4,6-tris(trifluoromethyl)thiophenol[33] (TFTP) was investigated as a potential polarity-reversal catalyst for hydroacylation and hydrosilylation reactions of alkenes. The results are included in Table 3 and show clearly that TFTP is an effective catalyst for both types of radical-chain addition and is comparable with TDT.

These preliminary experiments with TFTP indicate that it should be possible to use steric and electronic ring-substituent effects to tailor the properties of an arenethiol for a particular catalytic application.

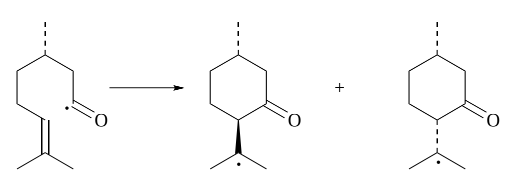
Cyclisation of unsaturated aldehydes

There are several reports in the literature of the cyclisation of unsaturated aldehydes under free-radical conditions.[16,17] Intramolecular addition of an acyl radical to a C=C bond benefits from the usual advantage of intra- over inter-molecular addition processes and, for medium-sized rings, is rapid even for unactivated alkene functions.[3,34] However, the overall hydroacylation reaction still suffers from short chain-lengths, because of slow abstraction of hydrogen from the aldehyde function by the cyclic adduct radical.

In order to investigate the effect of thiol catalysis on the intramolecular hydroacylation of unsaturated aldehydes, we chose to focus on the cyclisation of (*S*)-(−)-citronellal **40**.[16] In 1965 Monthéard[16a] reported that a mixture of menthone **41** (40%) and isomenthone **42** (20%) was obtained when diacetyl



40 **41** **42**



43 **44** **45**

(13)

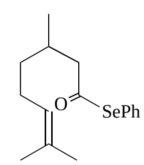
Table 4 Cyclisation of (*S*)-(−)-citronellal **40** in dioxane at 60 °C[a]

Thiol catalyst[b]	Yield of menthone + isomenthone (%)	Menthone : isomenthone
None	8	57 : 43
TDT	45	57 : 43
MTG	30	57 : 43
Pr^i_3SiSH	75	58 : 42
Ph_3SiSH	70	58 : 42
TFTP	40	58 : 42

[a] Reactions were initiated with TBHN (4 × 2.5 mol%). [b] Added in two portions (2 × 5 mol%).

peroxide (amount unspecified) was added in small portions to a 10% solution of citronellal in hexane (bp 69 °C) heated under reflux.†† The detailed reaction conditions were not given but, in our hands, portionwise addition of diacetyl peroxide (1.5 mmol, for safety reasons as a 50% w/v solution in dimethyl phthalate) during 1 h to a refluxing solution of (*S*)-(−)-citronellal (2.5 mmol) in hexane (3 cm^3), followed by further heating under reflux for 5 h, afforded menthone and isomenthone (58 : 42) in a total yield of 24%; the majority of the citronellal was recovered unchanged. Kampmeier *et al.*[16b] reported that the cyclisation of citronellal, initiated with dibenzoyl peroxide (10–20 mol%), either neat or in benzene at 80–100 °C, afforded a 2 : 1 mixture of menthone and isomenthone in a total yield of 15–19%; about 70% of the original aldehyde was recovered unchanged. The unsaturated acyl radical **43** evidently undergoes 6-*exo* ring closure to give the cyclic β-acylalkyl radicals **44** and **45**, with the (presumably) more stable *trans*-isomer **44** predominating, but chain transfer by abstraction of hydrogen from the aldehyde is slow.

Boger and Mathvink[2d] obtained **41** and **42** in a total yield of 80% by treatment of the acyl phenyl selenide **46** with tributyltin hydride (slow addition) at 80 °C; the *trans* : *cis* (menthone : isomenthone) product ratio was reported to be 56 : 44.



46

The radical-chain cyclisation of citronellal was examined under the usual conditions (TBHN, 4 × 2.5 mol%; thiol, 2 × 5 mol%; 3.5 h) in dioxane at 60 °C. Traces of acid appear to be produced by this combination of initiator and thiol and calcium carbonate (8 mol%) was added to the reaction mixtures to inhibit the acid-catalysed cyclisation of citronellal which otherwise afforded isopulegol and neoisopulegol as by-products.[35] Under these mild conditions the combined yield of menthone and isomenthone was only 8% in the absence of thiol, while in its presence yields of up to 75% were obtained, depending on the nature of the catalyst. The silanethiols were the most effective, as they are for the related radical-chain intramolecular hydrosilylation reactions.[36] The results are collected in Table 4.

Comparison with thiol-catalysed hydrosilylation of alkenes

There are many chemical similarities between RC(O)- and R_3Si-groups. Thiol-catalysis is often more effective for the radical-chain hydrosilylation of alkenes[23d,e] than for their hydroacylation, despite the fact that the RC(O)–H bond in an aldehyde (374 kJ mol^{-1} in acetaldehyde)[30] is weaker than the Si–H bond in a trialkylsilane (398 kJ mol^{-1} in Et_3SiH) or in a dialkylarylsilane (*ca.* 390 kJ mol^{-1} in $PhMe_2SiH$).[37] Addition of triorgano-

†† The structural formulae of menthone (the *trans*-isomer) and isomenthone (the *cis*-isomer) are reversed in Monthéard's paper.

silyl radicals to C=C bonds is generally faster[37] than addition of acyl radicals[12] and, unlike the latter reaction, seldom constitutes a bottleneck in the chain process. The electron-donor properties of a β-C–Si bond probably make an adduct radical of the type $R_3Si{-}\overset{|}{\underset{|}{C}}{-}\dot{C}{<}$ more nucleophilic than the corresponding acyl-radical adduct $RC(O){-}\overset{|}{\underset{|}{C}}{-}\dot{C}{<}$, facilitating hydrogen abstraction from the thiol catalyst by the former radical. It is only when hydrogen-atom abstraction by the thiyl radical from the aldehyde or from the silane becomes overall rate-controlling that the relative weakness of the aldehydic C–H bond could result in thiol-catalysed hydroacylation becoming the more favourable addition process.

Experimental

NMR spectra were recorded using a Varian VXR-400 instrument (400 MHz for ^{1}H). The solvent was $CDCl_3$ and chemical shifts are reported relative to Me_4Si; *J* values are quoted in Hz. Column chromatography and TLC were carried out using Merck Kieselgel 60 (230–400 mesh) and Kieselgel 60 F_{254} aluminium-backed pre-coated plates, respectively. All manipulations and reactions of air-sensitive compounds were carried out under an atmosphere of dry argon or nitrogen and all extracts were dried over anhydrous $MgSO_4$. Petroleum refers to the fraction of bp 40–60 °C. $[a]_D$ Values are given in 10^{-1} deg $cm^2\ g^{-1}$.

Materials

Dioxane was heated under reflux over calcium hydride and distilled and stored under argon. All the aldehydes and commercially available alkenes were freshly distilled under argon before use. TBHN was prepared by the reaction of sodium hyponitrite with *tert*-butyl bromide in diethyl ether, in the presence of zinc chloride, using the method described by Mendenhall.[25b–d]

(*S*)-(−)-Citronellal (Acros) was redistilled before use; it showed $[a]_D^{22}$ −18.4 (*c* = 2.44, $CHCl_3$), corresponding to an enantiomeric excess of *ca.* 94%.[38]

Triisopropylsilanethiol[27] and 2,4,6-tris(trifluoromethyl)thiophenol (TFTP)[33] (bp 62–64 °C/15 Torr) were prepared by published methods; other thiols were obtained commercially (Aldrich) and were used without further purification.

The enol ester **5c**,[39] the silyl enol ether **5d**[40] (bp 135 °C), the enol phosphate **5f**[41] (bp 57 °C/0.6 Torr), the α-methylene carbonate **12**,[42] 2-methylallyl acetate[43] **18** and the vinylsilanes[44] **36** and **37** were prepared by methods described in the literature.

The methylene lactone **11**[45] was prepared by acid-catalysed dehydration of 4,4-dimethyl-5-oxohexanoic acid using isopropenyl acetate and following a published procedure[46] used for similar compounds; bp 42–44 °C/0.05 Torr (lit.,[45] bp 95–96 °C/10 Torr); δ_H 1.19 (6H, s, 2Me), 1.67 (2H, t, *J* 7.1, CH_2), 2.64 (2H, t, *J* 7.1, CH_2), 4.32 (1H, d, *J* 1.8, vinyl), 4.60 (1H, d, *J* 1.8, vinyl); δ_C 26.3, 27.6, 32.3, 33.0, 91.9, 163.5, 168.4 (C=O).

2-Oxo-6-methyl-3,4-dihydro-2*H*-pyran[47] **13** was prepared by the acid-catalysed dehydration of 5-oxohexanoic acid with isopropenyl acetate following the published procedure,[45] bp 82–84 °C/15 Torr (lit.,[47] 100 °C/40 Torr); δ_H 1.86 (3H, d, *J* 1.5, Me), 2.26 (2H, m), 2.55 (2H, t, *J* 7.5, CH_2), 4.98 (1H, m, vinyl); δ_C 18.6, 28.3 (2C), 100.0, 150.0, 169.2 (C=O).

Dimethyl (2-methylallyl)malonate[48] **16** was prepared from 2-methylallyl chloride and dimethyl sodiomalonate, itself prepared by deprotonation of dimethyl malonate with sodium methoxide in methanol.

Butanoyl phenyl selenide[49] was prepared from butyric acid and phenylselenenyl chloride, using Crich's method,[50] as a pale yellow oil; δ_H 1.01 (3H, t, *J* 7.4, Me), 1.75 (2H, m, CH_2), 2.72 (2H, t, *J* 7.3, CH_2), 7.41 (3H, m, Ar), 7.48 (2H, m, Ar); δ_C 13.3, 18.9, 49.3, 126.4, 128.7, 129.2, 135.7, 200.3 (C=O). Hydroacylations using the butanoyl phenyl selenide–tributyltin hydride couple were carried out in refluxing benzene with AIBN (10 mol%) initiator, as described by Boger and Mathvink;[2d] the tin hydride was added to the reaction mixture during 1.5 h using a motor-driven syringe pump.

Typical procedure for the reactions of electron-rich alkenes with aldehydes

A solution of isopropenyl acetate (**5a**, 0.25 g, 2.5 mmol), butanal (**4a**, 0.45 cm^3, 5.0 mmol) and TBHN (11 mg, 2.5 mol%, based on **5a**) in dioxane (2.5 cm^3) in a small flat-bottomed flask, containing a magnetic stirrer bar and fitted with a short reflux condenser, was briefly purged with a stream of argon through a side arm in the flask, which was then closed with a stopper. The flask was then placed in an oil bath which had been preheated to 60 °C and methyl thioglycolate (MTG, 12 µl, 5 mol% based on **5a**) was added quickly through the side arm. Further amounts of TBHN (2.5 mol%) and MTG (5 mol%) were added after 1 h and the solution was stirred under argon for a total of 3 h. The reaction mixture was allowed to cool, volatile material was removed at room temperature under reduced pressure (10–15 Torr). Methyl benzoate was added as an internal standard if the yield was to be estimated by ^{1}H NMR spectroscopy. The product was isolated by chromatography on silica gel using petroleum–diethyl ether (5:1 v/v) as eluent, to give 2-acetoxyheptan-4-one **6aa** (0.29 g, 67%) as a clear oil; δ_H 0.86 (3H, t, *J* 8.1, Me), 1.22 (3H, d, *J* 6.3, Me), 1.56 (2H, m, CH_2), 1.96 (3H, s, Ac), 2.35 (2H, t, *J* 7.3, CH_2), 2.48 (1H, dd, *J* 16.3 and 5.9, 3-H), 2.74 (1H, dd, *J* 16.3 and 7.1, 3-H), 5.24 (1H, m, 2-H); δ_C 13.6, 16.9, 20.0, 21.1, 45.2, 48.4, 67.1, 170.2, 207.7 (C=O) (Found: C, 62.6; H, 9.3. $C_9H_{16}O_3$ requires C, 62.8; H, 9.4%). Other addition reactions of **5a**–**g** were carried out in a similar way and the characteristics of the products are given below; the yields are given in Table 1.

1-Acetoxyhexan-3-one 6ab. Oil; δ_H 0.89 (3H, t, *J* 7.3, Me), 1.60 (2H, m, CH_2), 1.99 (3H, s, Ac), 2.39 (2H, t, *J* 7.3, CH_2), 2.70 (2H, t, *J* 6.3, CH_2), 4.30 (2H, t, *J* 6.3, OCH_2); δ_C 13.6, 17.0, 20.8, 41.2, 45.1, 59.3, 170.8, 207.9 (C=O) (Found: C, 60.5; H, 9.0. $C_8H_{14}O_3$ requires C, 60.7; H, 8.9%).

The 'dimeric' by-product 8. Oil; δ_H 0.86 (3H, t, *J* 7.4, Me), 1.54 (2H, m, CH_2), 1.91 (2H, m, CH_2), 1.98 (3H, s, Ac), 2.01 (3H, s, Ac), 2.36 (2H, t, *J* 7.3, CH_2), 2.58 (1H, dd, *J* 16.5 and 6.2, 7-H), 2.76 (1H, dd, *J* 16.5 and 6.8, 7-H), 4.08 (2H, t, *J* 6.4, 8-H), 5.31 (1H, m, 6-H); δ_C 13.6, 17.0, 20.93, 21.03, 32.9, 45.3, 46.7, 60.5, 67.5, 170.3, 171.0, 207.4 (C=O) (Found: C, 59.1; H, 8.3. $C_{12}H_{20}O_5$ requires C, 59.0; H, 8.3%).

6-Acetoxy-7,7-dimethyloctan-4-one 6ac. Oil; δ_H 0.88 (3H, t, *J* 7.4, Me), 0.89 (9H, s, CMe_3), 1.56 (2H, m, CH_2), 2.00 (3H, s, Ac), 2.40 (2H, m, CH_2), 2.55 (2H, m, CH_2), 5.13 (1H, dd, *J* 8.5 and 4.0, 6-H); δ_C 13.7, 17.1, 21.0, 25.8, 34.5, 43.5, 44.9, 76.3, 170.4, 208.5 (C=O) (Found: C, 67.2; H, 10.4. $C_{12}H_{22}O_3$ requires C, 67.3; H, 10.4%).

1-(*tert*-Butyldimethylsiloxy)hexan-3-one 6ad. Oil; δ_H 0.04 (6H, s, $SiMe_2$), 0.87 (9H, s, CMe_3), 0.89 (3H, t, *J* 7.5, Me), 1.59 (2H, m, CH_2), 2.42 (2H, t, *J* 7.2, CH_2), 2.58 (2H, t, *J* 6.2, CH_2), 3.88 (2H, t, *J* 6.2, OCH_2); δ_C 0.20, 13.7, 16.9, 25.8, 27.8, 45.6, 45.8, 58.9, 210.2 (C=O) (Found: C, 62.6; H, 11.4. $C_{12}H_{26}O_2Si$ requires C, 62.6; H, 11.4%).

6-(Trimethylsiloxy)-7,7-dimethyloctan-4-one 6ae. Oil; δ_H 0.06 (9H, s, $SiMe_3$), 0.83 (9H, s, CMe_3), 0.91 (3H, t, *J* 7.4, Me), 1.59 (2H, m, CH_2), 2.33–2.44 (3H, m), 2.55 (1H, dd, *J* 16.3 and 8.7, 5-H), 3.92 (1H, dd, *J* 8.7 and 2.7, 6-H); δ_C 0.42, 13.7, 16.9, 26.0, 35.0, 46.0, 46.5, 76.0, 210.3 (C=O) (Found: C, 63.7; H, 11.5. $C_{13}H_{28}O_2Si$ requires C, 63.9; H, 11.6%).

(Diethoxyphosphinoyloxy)heptan-4-one 6af. Viscous oil; δ_H 0.88 (3H, t, *J* 7.4, Me), 1.30 (6H, m, 2Me), 1.36 (3H, d, *J* 6.3, Me), 1.57 (2H, m, CH_2), 2.39 (2H, t, *J* 7.3, CH_2), 2.55 (1H, ddd, *J* 16.6, 6.5 and 1.7, 3-H), 2.88 (1H, dd, *J* 16.6 and 6.5, 3-H), 4.06 (4H, m, $2CH_2O$), 4.88 (1H, m, 2-H); δ_C 13.6, 16.1 (d, separation 6.9 Hz), 17.0, 21.8 (J_{C-P} 3.1), 45.5, 50.0 (J_{C-P} 6.0), 63.7 (m), 71.7

(J_{C-P} 6.2), 207.6 (C=O) (Found: C, 49.9; H, 8.8. $C_{11}H_{23}O_5P$ requires C, 49.6; H, 8.7%).

1-Butoxyhexan-3-one 6ag. Oil; δ_H 0.90 (6H, 2 sets of t, *J* 7.6 and 7.3, 2Me), 1.33 (2H, m, CH_2), 1.52 (2H, m, CH_2), 1.59 (2H, m, CH_2), 2.41 (2H, t, *J* 7.3, CH_2), 2.63 (2H, t, *J* 6.4, CH_2), 3.40 (2H, t, *J* 6.5, CH_2), 3.65 (2H, t, *J* 6.2, CH_2); δ_C 13.7, 13.9, 17.0, 19.3, 31.7, 42.9, 45.3, 65.8, 70.9, 209.7 (C=O) (Found: C, 69.8; H, 11.7. $C_{10}H_{20}O_2$ requires C, 69.7; H, 11.7%).

2-Acetoxyundecan-4-one 6ba.[51] Oil; δ_H 0.85 (3H, t, *J* 6.3, Me), 1.24 (11H, m), 1.54 (2H, m, CH_2), 1.99 (3H, s, Ac), 2.34 (2H, t, *J* 7.4, CH_2), 2.51 (1H, dd, *J* 16.3 and 5.9, 3-H), 2.75 (1H, dd, *J* 16.3 and 7.1, 3-H), 5.26 (1H, m, 2-H); δ_C 14.1, 20.1, 21.1, 22.6, 23.6, 29.07, 29.12, 31.7, 43.4, 48.5, 62.7, 170.3, 207.9 (C=O) (Found: C, 68.5; H, 10.6. $C_{13}H_{24}O_3$ requires C, 68.4; H, 10.6%).

2-Acetoxy-6-methylheptan-4-one 6ca. Oil; δ_H 0.89 (6H, d, *J* 6.6, 2Me), 1.24 (3H, d, *J* 6.4, Me), 1.98 (3H, s, Ac), 2.11 (1H, m, 6-H), 2.26 (2H, d, *J* 6.7, 5-H), 2.48 (1H, dd, *J* 16.4 and 5.9, 3-H), 2.74 (1H, dd, *J* 16.4 and 7.3, 3-H), 5.26 (1H, m, 2-H); δ_C 20.0 (2C), 21.2, 22.4, 24.4, 48.9, 52.3, 67.1, 170.2, 207.4 (C=O) (Found: C, 64.6; H, 9.9. $C_{10}H_{18}O_3$ requires C, 64.5; H, 9.7%).

2-Acetoxy-6,8,8-trimethylnonan-4-one 6da. Oil, as an approximately equal mixture of two diastereoisomers; δ_H(both diastereoisomers) 0.88 (9H, s, CMe_3), 0.89 (3H, d, *J* 7.6, Me), 1.11 (2H, m, CH_2), 1.24 (3H, d, *J* 6.2, Me), 1.95 (3H, s, Ac), 2.09 (1H, m, 6-H), 2.23 (1H, m, 5-H), 2.38 (1H, m, 5-H), 2.46 (1H, m, 3-H), 2.74 (1H, m, 3-H), 5.26 (1H, m, 2-H); δ_C(bracketed pairs arise from diastereoisomers) 20.1, 21.2, (22.68 and 22.73), (25.67 and 25.70), 30.1, 31.1, (48.99 and 49.05), (50.85 and 50.88), (53.05 and 53.08), 67.2, 170.2, 207.5 (C=O) (Found: C, 69.5; H, 10.8. $C_{14}H_{26}O_3$ requires C, 69.4; H, 10.8%).

2-Acetoxy-6,11-dimethyl-11-methoxydodecan-4-one 6ea. Viscous oil, as an approximately equal mixture of two diastereoisomers; δ_H(both diastereoisomers) 0.870 and 0.874 (3H, 2 sets of d, *J* 7.4, 6-Me), 1.11 (6H, s, 11- and 12-Me), 1.241 and 1.246 (3H, 2 sets of d, *J* 6.4, 1-Me), 1.10–1.45 (8H, m), 1.90 (1H, m, 6-H), 1.99 (3H, s, Ac), 2.20 (1H, m, 5-H), 2.38 (1H, m, 5-H), 2.48 (1H, m, 3-H), 2.76 (1H, m, 3-H), 3.15 (3H, s, OMe), 5.26 (1H, m, 2-H); δ_C(both diastereoisomers) 19.70, 19.75, 20.0, 24.92, 24.95, 29.0, 37.31, 37.35, 39.9, 48.95, 48.98, 49.1, 50.76, 50.80, 67.07, 67.11, 74.5, 170.2, 207.53, 207.55 (C=O) (Found: C, 68.2; H, 10.8. $C_{17}H_{32}O_4$ requires C, 68.0; H, 10.7%).

***N*-(3-Oxohexyl)-2-pyrrolidone 9.** Oil; δ_H 0.88 (3H, t, *J* 7.4, Me), 1.57 (2H, m, CH_2), 2.33 (2H, t, *J* 8.4, CH_2), 2.38 (2H, t, *J* 7.2, CH_2), 2.67 (2H, t, *J* 6.7, CH_2), 3.39 (2H, t, *J* 7.2, CH_2), 3.50 (2H, t, *J* 6.7, CH_2); δ_C 13.6, 17.0, 18.0, 30.9, 37.7, 40.4, 44.7, 48.1, 175.3, 209.3 (C=O) (Found: C, 65.8; H, 9.4; N, 7.4. $C_{10}H_{17}NO_2$ requires C, 65.5; H, 9.4; N, 7.6%).

***N*-(3-Oxohexyl)phthalimide 10.** Mp 56 °C (from CH_2Cl_2–petroleum); δ_H 0.84 (3H, t, *J* 7.4, Me), 1.55 (2H, m, CH_2), 2.36 (2H, t, *J* 7.2, CH_2), 2.79 (2H, t, *J* 7.4, CH_2), 3.89 (2H, t, *J* 7.4, CH_2), 7.55–7.90 (4H, m, Ar); δ_C 13.7, 17.1, 33.0, 40.6, 44.3, 123.2, 132.0, 134.0, 168.1, 208.2 (C=O) (Found: C, 68.8; H, 6.3; N, 5.5. $C_{14}H_{15}NO_3$ requires C, 68.6; H, 6.2; N, 5.7%).

4,4-Dimethyl-5-(2-oxopentyl)-1,3-dioxolan-2-one 14. This compound decomposed on silica gel during attempted purification; δ_H 0.93 (3H, t, *J* 7.4, Me), 1.35 (3H, s, Me), 1.58 (3H, s, Me), 1.62 (2H, m, CH_2), 2.47 (2H, m, CH_2), 2.69 (1H, dd, *J* 17.5 and 6.4), 2.95 (1H, dd, *J* 17.5 and 7.0), 4.83 (1H, t, *J* 6.7).

General procedure for the reactions of electron-deficient alkenes with aldehydes

The reactions of the electron-deficient alkenes with aldehydes were carried out under similar conditions to those described above for electron-rich alkenes, except that the TBHN initiator (10 mol%) was added in four equal portions of 2.5 mol%; one was present at the start of the reaction and the other three were added at intervals of 30 min during the first 1.5 h; the total reaction time was 3.5 h. The products were isolated by chromatography on silica gel using appropriate mixtures of petroleum–diethyl ether as eluent. The yields are given in Scheme 2 and in the text; the characteristics of the adducts are given below.

Ethyl 2-ethoxycarbonyl-6-oxononanoate 21.[52] Oil; δ_H 0.89 (3H, t, *J* 7.4, Me), 1.25 (6H, t, *J* 7.2, 2Me), 1.58 (4H, m, $2CH_2$), 1.85 (2H, m, CH_2), 2.34 (2H, t, *J* 7.3, CH_2), 2.42 (2H, t, *J* 7.3, CH_2), 3.31 (1H, t, *J* 7.3), 4.17 (4H, q, *J* 7.2, $2CH_2O$); δ_C 13.7, 14.0, 17.2, 21.4, 28.2, 42.1, 44.7, 51.9, 61.4, 169.2, 210.3 (C=O).

Methyl 2-methoxycarbonyl-4-methyl-6-oxononanoate 22. Oil; δ_H 0.89 (3H, t, *J* 6.9, Me), 0.90 (3H, d, *J* 6.6, Me), 1.57 (2H, m, CH_2), 1.74 (1H, m), 1.90 (1H, m), 2.00 (1H, m), 2.24 (1H, dd, *J* 16.3 and 7.9), 2.34 (2H, t, *J* 7.6), 2.38 (1H, dd, *J* 16.3 and 5.3), 3.43 (1H, dd, *J* 8.5 and 7.0), 3.72 (3H, s, OMe), 3.74 (3H, s, OMe); δ_C 13.7, 17.1, 19.4, 27.1, 35.6, 45.2, 49.6, 49.7, 52.6, 169.8, 209.9 (C=O) (Found: C, 60.7; H, 8.6. $C_{13}H_{22}O_5$ requires C, 60.5; H, 8.6%).

Ethyl 6-oxononanoate 23.[53] Oil; δ_H 0.89 (3H, *J* 7.4, Me), 1.23 (3H, t, *J* 7.2, Me), 1.59 (6H, m), 2.35 (6H, m), 4.11 (2H, q, *J* 7.2, OCH_2); δ_C 13.7, 14.2, 17.2, 23.2, 24.5, 34.1, 42.3, 44.7, 60.2, 173.4, 210.7 (C=O).

1-Acetoxy-2-methylheptan-4-one 24.[54] Oil; δ_H 0.92 (6H, m due to overlap, 2- and 7-Me), 1.58 (2H, m, CH_2), 2.03 (3H, s, Ac), 2.25 (1H, dd, *J* 16.1 and 7.2, 3-H), 2.36 (2H, t, *J* 7.0, CH_2), 2.39 (1H, m, 2-H), 2.48 (1H, dd, *J* 16.1 and 5.6, 3-H), 3.86 (1H, dd, *J* 10.8 and 6.5, 1-H), 3.94 (1H, dd, *J* 10.8 and 5.8, 1-H); δ_C 13.7, 16.9, 17.2, 20.9, 28.6, 45.3, 46.4, 68.6, 171.0, 209.7 (C=O).

1,1-Diacetoxy-2-methylheptan-4-one 25. Oil; δ_H 0.90 (3H, t, *J* 7.6, Me), 0.94 (3H, d, *J* 6.7, Me), 1.59 (2H, m, CH_2), 2.04 (3H, s, Ac), 2.07 (3H, s, Ac), 2.27 (1H, dd, *J* 16.6 and 7.8, 3-H), 2.37 (2H, m, CH_2), 2.53 (1H, m, 2-H), 2.59 (1H, dd, *J* 16.6 and 5.0, 3-H), 6.67 (1H, d, *J* 4.0, 1-H); δ_C 13.7, 14.3, 17.2, 20.7, 32.1, 43.5, 45.2, 91.6, 168.9, 208.9 (C=O) (Found: C, 59.2; H, 8.3. $C_{12}H_{20}O_5$ requires C, 59.0; H, 8.3%).

2-(3-Oxohexyl)-1,3-dioxolane 26. Oil; δ_H 0.89 (3H, t, *J* 7.40, Me), 1.58 (2H, m, CH_2), 1.95 (2H, m, CH_2), 2.38 (2H, t, *J* 7.5, CH_2), 2.51 (2H, t, *J* 7.6, CH_2), 3.82 (2H, br s, OCH_2), 3.93 (2H, br s, OCH_2), 4.88 (1H, m, 2-H); δ_C 13.8, 17.3, 27.6, 36.5, 44.7, 65.0, 103.4, 210.1 (C=O) (Found: C, 62.5; H, 9.4. $C_9H_{16}O_3$ requires C, 62.8; H, 9.4%).

Ethyl 3-methyl-4-oxoheptanoate 28. Oil; δ_H 0.90 (3H, t, *J* 7.4, Me), 1.11 (3H, d, *J* 7.2, Me), 1.22 (3H, t, *J* 7.4, Me), 1.60 (2H, m, CH_2), 2.26 (1H, dd, *J* 16.7 and 5.3, 2-H), 2.49 (2H, m, CH_2), 2.75 (1H, dd, *J* 16.7 and 8.9, 2-H), 2.98 (1H, m, 3-H), 4.08 (2H, q, *J* 7.4, $2CH_2O$); δ_C 13.7, 14.1, 16.7, 17.0, 37.0, 42.0, 43.1, 60.5, 172.3, 212.9 (C=O) (Found: C, 64.6; H, 9.6. $C_{10}H_{18}O_3$ requires C, 64.5; H, 9.7%).

Ethyl 3-ethoxycarbonyl-4-oxoheptanoate 31.[14a] Oil; δ_H 0.91 (3H, m, Me), 1.25 (6H, m, 2Me), 1.63 (2H, m, CH_2), 2.65 (2H, m, CH_2), 2.81 (1H, m), 2.95 (1H, m), 3.96 (1H, m), 4.11 (2H, m, OCH_2), 4.18 (2H, m, OCH_2); δ_C 14.1, 16.9, 32.4, 44.7, 54.0, 61.0, 61.8, 168.5, 171.4, 204.0 (C=O).

3-Oxohexyl phenyl sulfone 33. Viscous oil; δ_H 0.87 (3H, t, *J* 7.4, Me), 1.56 (2H, m, CH_2), 2.39 (2H, t, *J* 7.3, CH_2), 2.88 (2H, t, *J* 7.4, CH_2), 3.37 (2H, t, *J* 7.3, CH_2), 7.52 (2H, m, Ar), 7.66 (1H, m, Ar), 7.89 (2H, m, Ar); δ_C 13.6, 17.1, 34.8, 44.6, 50.5, 127.9, 129.3, 133.9, 139.9, 206.1 (C=O) (Found: C, 60.2; H, 6.8. $C_{12}H_{16}O_3S$ requires C, 60.0; H, 6.7%).

1-Trimethylsilyldecan-3-one 35. This compound decomposed on silica gel during attempted purification; δ_H −0.05 (9H, s, $SiMe_3$), 0.73 (2H, m, CH_2), 0.84 (3H, m, Me), 1.27 (10H, m, $5CH_2$), 2.35 (2H, m, CH_2), 2.40 (2H, m, CH_2).

Ethyl 4-(4-methoxyphenyl)-3-methyl-4-oxobutanoate 38b.[2d] Oil; δ_H 1.15 (3H, d, *J* 7.3, Me), 1.23 (3H, t, *J* 7.1, Me), 2.30 (1H, dd, *J* 16.5 and 7.3), 2.81 (1H, dd, *J* 16.5 and 8.5), 3.04 (1H, m), 3.90 (3H, s, OMe), 4.11 (2H, q, *J* 7.1, OCH_2), 6.95 (2H, d, *J* 8.7, Ar), 7.98 (2H, d, *J* 8.7, Ar); δ_C 17.5, 33.3, 42.2, 43.5, 60.9, 61.8, 114.1, 128.5, 136.6, 163.9, 172.3, 192.8 (C=O).

Ethyl 3-ethoxycarbonyl-4-(4-methoxyphenyl)-4-oxobutanoate 39.[14a,55] Oil; δ_H 1.14 (3H, t, *J* 7.1, Me), 1.20 (3H, t, *J* 7.1, Me), 3.00 (2H, m), 3.85 (3H, s, OMe), 4.10 (4H, m, $2CH_2O$), 4.79 (1H, t, *J* 7.1), 6.92 (2H, d, *J* 8.7, Ar), 7.99 (2H, d, *J* 8.7, Ar); δ_C

13.9, 14.1, 33.3, 49.3, 55.5, 60.9, 61.7, 113.9, 128.8, 131.3, 164.0, 168.9, 171.3, 192.4 (C=O) (Found: C, 62.6; H, 6.6. $C_{16}H_{20}O_6$ requires C, 62.3; H, 6.5%).

Typical procedure for radical-chain cyclisation of citronellal

A mixture of (*S*)-(−)-citronellal (0.39 g, 2.5 mmol), TBHN (11 mg, 2.5 mol%), triisopropylsilanethiol (29 µl, 24 mg, 5 mol%) and $CaCO_3$ (20 mg, 8 mol%) in dioxane (2.5 cm^3) was stirred at 60 °C under argon. TBHN (3 × 2.5 mol%) was added at 30 min intervals during the first 1.5 h and more thiol (5.0 mol%) was added after 1 h; the reaction mixture was heated for 3.5 h in all. The yield and the isomer ratio **41**:**42** were determined by ^1H NMR spectroscopy and GLC analysis by comparison with authentic samples of menthone and isomenthone (the latter prepared by the oxidation of isomenthol[56]); the results are given in Table 4.

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